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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/520,341 | 10/20/2005 | Jian Liu | 421/67 PCT/US | 2710 |

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| EXAMINER | |
|---|---|
| SHEN, WU CHENG WINSTON | |
| ART UNIT | PAPER NUMBER |
| 1632 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/520,341 | **Applicant(s)** LIU ET AL. | |
|---|---|---|---|
| | **Examiner** WU-CHENG Winston SHEN | **Art Unit** 1632 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 29 July 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-4*.
   Claim(s) withdrawn from consideration: *5-60*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632

Continuation of 5.

Applicant's arguments in combination with claim amendments filed on 07/29/2008 have overcome the rejection of claims 1-4 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner notes that the withdrawal of this written description is based on the recently revised Written Description Training Materals available online http://www.uspto.gov/web/menu/written.pdf, which Applicant refers to as "the WDTM" in the After-Final response filed on 07/29/2008 (See page 13 of Applicant's after-Final response). Furthermore, the Examiner have reconsidered the Enzo and Adler case laws cited by Applicant with respect to whether Applicant's had the possession of the claimed invention pertaining to heparin sulfate 3-O-sulfotransferase 5 polypeptide having greater than 95% sequence identity to SEQ ID NO:2 (recited in claim 1), a polypeptide encoded by a nucleic acid sequence as set forth in SEQID NO 1 (recited in claim 2);and a polypeptide having an amino acid sequence as set forth in SEQ ID NO 2 (recited in claim 2), and the polypeptide of claim 1, wherein the polypeptide is a human heparan sulfate 3-O-sulfotransferase 5 polypeptide (recited in claim 3).

Applicant's arguments in combination with claim amendments filed on 07/29/2008 have overcome the rejection of claim 2 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for an isolated and purified biologically active heparan sulfate 3-O-sulfotransferase 5 polypeptide wherein the polypeptide catalyzes the reactions generating at least three 3-O-sulfated disaccharides as follows: IdoUA2-AnMan3S, GlcUA-AnMan3S6S, and IdoUA2S-AnMan3S6S, does not reasonably provide enablement for (4) any polypeptide encoded by a nucleic acid molecule capable of hybridizing under stringent conditions to a nucleic acid molecule comprising the nucleotides of SEQ ID NO 1, or a complement thereof. The aspect (4) of the rejection is moot because of the claim amendments filed on 07/29/2008 deletes the previous limitation (d) recited in claim 2.

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant's arguments have failed to overcome the rejection of claims 1-4 as amended under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified biologically active heparan sulfate 3-O-sulfotransferase 5 polypeptide wherein the polypeptide catalyzes the reactions generating at least three 3-O-sulfated disaccharides as follows: IdoUA2-AnMan3S, GlcUA-AnMan3S6S, and IdoUA2S-AnMan3S6S, does not reasonably provide enablement for (1) any fragment or variant of polypeptide encoded by a nucleic acid sequence as set forth in SEQ ID NO 1; (2) any fragment of a polypeptide encoded by a nucleic acid sequence having greater than 95% but less than 100% sequence identity of SEQ ID No 1; (3) any fragment of polypeptide having an amino acid sequence having greater than 95% sequence identity of SEQ ID NO 2.

The essence of Applicant's arguments filed 07/29/2008 is the same as the arguments filed on 01/14/2008, which has been responded in details on pages 20-21 in the Final office action mailed on 04/29/2008. Applicant argues, in particular, that the genus of the claimed 3-OST-5 is at least 95% identical to SEQ ID NO 2, and the specification discloses the complete sequence of nucleic acids encoding the protein of SEQ ID NO 2, assays to determine whether the modified protein possesses 3-OST-5 activity (see, e.g., Examples 2-9), and guidance to make the appropriate amino acid modifications provided by the sequence comparison in Figure 2 showing conserved and less conserved regions between the 3-OST isozymes, 3-OST-1,3-OST-3A, 3-OST-3B and 3-OST-5 (See third paragraph, page 19 of Applicant's response filed on 07/29/2008.

In response, the Examiner maintains the position that the specification fails to provide correlation between structure and function of fragments encompassed by the broad genus of 3-OST-5 polypeptide. An artisan would not know which 5% of the sequence could be different from any fragment of the polypeptide sequence of SEQ ID NO: 2 and still retain the function of the claimed 3-OST-5 biological activity. Disclosure of which 5% of the sequence and possible variations could be different from any fragment of the polypeptide sequence of SEQ ID NO: 2 is particularly important for the enablement of any fragment encompassed by claims 1-4 because the specification specifically points out that "the substrate specificity of 3-OST isoforms are determined by the three-dimensional structures of the enzymes" (See paragraph [0059], US PGPUB 2006/016/0165673, publication of instant application). Furthermore, the status of art indicates that a single point mutations such as R72A, R67A, and K123A result in 3-OST-1 (a 307 animo-acid long polypeptide for human 3-OST-1) mutants that are inactive (See page 14 of Non-Final office action mailed on 07/12/2007). Therefore, it is unpredictable whether 5% difference from claimed SEQ ID No:2 of instant application can be biological active.